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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/542,935	04/04/2000	Maria Palasis	02844/56301	5876

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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/542,935	PALASIS, MARIA	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,10-12,17-20,23-25,27,34-38,42-44,47,54,55,58-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,10-12,17-20,23-25,27,34-38,42-44,54,55,58-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/12/04 has been entered.

Claims 3, 10-12, 17-20, 23-25, 27, 34-38, 42-44, 47, 54, 55, and 58-62 are pending.

The amendment filed on 4/12/04 is acknowledged and considered.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: the claims are unsupported under 35 U.S.C. 112, first paragraph, as failing to comply with the 112 first paragraph written description. The original specification (09/204,254 filed 12/3/98, now US 6,369,039) did not disclose making and using a medical device comprising a biocompatible structure carrying a genetic material, said biocompatible structure comprising a polymeric coating that coats at least a portion of said structure, said genetic material comprising: a therapeutic agent comprising an angiogenic agent; and cell cycle inhibitors; a vector containing a first polynucleotide encoding an angiogenic agent; and cell cycle inhibitors, and combinations thereof.

In addition, the '039 specification set forth a list of products that the vector and the carrier can carry (pages 16-19). However, the list set forth in the new claims does not include all of the products listed in the specification. The specification does not disclose the subgenus set forth in the new claims. Thus, nothing in the specification would lead one to the particular combination set forth in the new claims. "It is not sufficient for purposes of the written description requirement of Section 112 that the disclosure, when combined with the knowledge in the art, would lead one to speculate as to modifications that the inventor might have envisioned, but failed to disclose." *Lockwood v. American Airlines Inc.,* 41 USPQ2d 1961, 1966 (CAFC 1997).

Applicant respectfully traverses and maintains that the '039 specification provides adequate support for the presently pending claims by explicitly guiding one of skill to combine a therapeutic agent and vector, as claimed in new independent claims 60 and 62 and claims dependent thereon. (Emphasis added) The original description of the '039 patent provides a specific written description for the particular combination of a therapeutic agent and a vector encoding a polypeptide or protein selected from the above-recited group, as claimed. (See Col. 4, lines 64-67; Col. 5, lines 1-44; and Col. 5, line 62 through Col. 6, line 7). One of skill is clearly guided by the original '039 specification to combine a therapeutic agent and a vector by the explicit teaching at Col. 5, lines 62-65 of "the polypeptides or proteins that can be incorporated into the polymer coating 130, or whose DNA can be incorporated, include without limitation, angiogenic factors..." ...and combinations thereof (See Col. 6, lines 7). Therefore, the '039 specification specifically lists the claimed therapeutic agents as well as polynucleotides encoding such therapeutic agents as being incorporated into the polymer coating and further clearly

provides for combinations of such polypeptides/proteins and DNA with the ending phrase "and combinations thereof', indicating that combinations of therapeutic agents (polypeptides/proteins) and vectors containing DNA encoding polypeptides/proteins may be combined in the coating.

The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter"' Vas-Cath, Inc. v. Mahurkar 935 F.2d 1555, 1563 (Fed. Cir. 1991) citing Ralston Purina Co. v. Far-Mar-co, Inc., 772 F.2d1 570, 1575, (quoting In re Kaslow, 707 F.2d 1366, 1375 (Fed.Cir. 1983)) (citations omitted) (Emphasis added).

Applicant's arguments filed 4/12/04 have been fully considered but they are not persuasive.

The argument is not found persuasive because in view of MPEP 2131.05 II and *Lockwood v. American Airlines Inc.,* 41 USPQ2d 1961, 1966 (CAFC 1997), the assertion "the application relied upon reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter"' is not supported by any evidence of record. Also see MPEP § 716.01(c). There is nothing in application that would reasonably lead one skilled to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 10-12, 17-20, 23-25, 27, 34-38, 42-44, 47, 54, 55, and 58-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New claims 60-62 filed on 4/12/04 introduce new subject matter into the application. In view of the election of species filed on 10/4/02, the application and the originally filed claim as a whole are directed to:

A medical device comprising (a) a first therapeutic agent comprising a vector containing a first polynucleotide; and (b) a second therapeutic agent comprising a non-genetic therapeutic agent.

With respect to new claims 60 and 62, the original specification did not disclose a medical device comprising a therapeutic agent consisting of an angiogenic agent; and cell cycle inhibitors; a vector containing a polynucleotide encoding an angiogenic agent; and cell cycle inhibitors; and combinations thereof. As set forth above, the originally filed claims provide support for a first therapeutic agent comprising a vector containing a first polynucleotide and a second therapeutic agent comprising a protein or a non-genetic therapeutic agent. The support cited for the newly added claims does not provide support for the new claims. Page 17, lines 6-9, states: "The first therapeutic agent of this invention comprises genetic materials whereas the second therapeutic agent of the invention may comprise either genetic or non-genetic material. The non-genetic material comprises any molecule or compound that induces a beneficial or medical reaction in vitro, or in vivo." Furthermore, page 17, line 20 through page 18, line 16 is

directed to list of anti-angiogenic and angiogenic agents. Claims 60 and 62 are directed to a subgenus of the genus listed on these pages. The specification does not disclose the subgenus set forth in the new claims. The specification does not disclose using one or two cell cycle inhibitors with an angiogenic agent or a vector comprising an angiogenic agent. The working examples in the specification are directed to using one vector comprising a marker gene or an angiogenic agent or two vectors comprising an angiogenic agent. It is apparent that the applicants at the time the invention was made did not intend or contemplate making an/or using the medical device set forth in the newly added claims as part of the disclosure of their invention. There is no evidence in the specification that the applicants were possession of the medical device as set forth in the newly filed claims and claims dependent thereof, as it is now claimed, at the time the application was filed.

In addition, with respect to newly filed claim 61, the original specification did not disclose a medical device comprising a therapeutic agent selected from the agents listed on lines 4-9 of new claim 61; a vector containing a polynucleotide encoding an angiogenic agent; and cell cycle inhibitors; and combinations thereof. Applicant claims that page 5, lines 3-10, page 17, lines 6-9, page 17, line 20 through page 18, lines 16. Page 5, lines 3-10, provides support for the originally filed claims and not the newly filed claim because page 5 recites the limitations set forth in claim 1. Page 17, lines 6-9, recites: "The first therapeutic agent of this invention comprises genetic materials whereas the second therapeutic agent of the invention may comprise either genetic or non-genetic material. The non-genetic material comprises any molecule or compound that induces a beneficial or medical reaction in vitro, or in vivo." This citation does not provide support for the newly filed claim. Page 17, line 20 through page 18, line 16 recites a

genus of agents and claim 61 recites a subgenus of the agents listed on these pages. In addition, the specification does not disclose which combinations to use. For example, tumor growth factor alpha is a procoagulant and a proinflammatory agent, See Dixit et al., J Biol Chem. 1990 15; 265:2973-8. The specification does not disclose why one skilled in the art would use an anticoagulant and a tumor growth factor alpha (procoagulant agent) on the same medical device. It is apparent that the applicants at the time the invention was made did not intend or contemplate making the medical device set forth in the newly added claims as part of the disclosure of their invention. There is no evidence in the specification that the applicants were possession of the medical device as set forth in the newly filed claim, as it is now claimed, at the time the application was filed.

Claims 3, 10-12, 17-20, 23-25, 27, 34-38, 42-44, 47, 54, 55, and 58-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Applicant claims a medical device comprising a therapeutic agent comprising an angiogenic agent; and cell cycle inhibitors; a vector containing a polynucleotide encoding an angiogenic agent; and cell cycle inhibitors; and combinations thereof and using the medical device in a method of controlled delivery.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reached by weighing many factors. These factors (In Re Wands Factors) are outlined above.

Applicants provide no working examples of the claimed invention. Applicants do demonstrate expressing a marker gene in arterial wall of mice using a stent, contemplate expressing NOS in vivo using an AAV vector, and contemplate expressing VEGF and a Fas ligand using two AAV vectors; however, neither the applicants nor the prior art provide a correlation or nexus between the results obtained in the working examples with results which the skilled artisan would reasonably expect from the combination set forth in the claimed invention.

The specification does not teach using a medical device comprising a therapeutic agent comprising an angiogenic agent; and cell cycle inhibitors; a vector containing a polynucleotide encoding an angiogenic agent; and cell cycle inhibitors; and combinations thereof. The prior art is absent for using the claimed medical device. The specification does not provide sufficient guidance and/or factual evidence for one skilled in the art to practice the claimed invention. The art of record teaches that a tumor growth factor alpha is a procoagulant and proinflammatory agent, See Dixit, supra. The specification and the prior art do not disclose how one skilled in the art would use an anticoagulant and a procoagulant in the same medical device. The specification contemplates using a genus of cell cycle inhibitors. The prior art teaches that cell cycle inhibitors inhibit angiogenesis, See Lee et al., J. Biol. Chem. 1998, 273:28805-12. The

specification does not teach using at least one cycle inhibitor, an angiogenic agent, a vector comprising an angiogenic agent. In the instant case, the combination set forth in the claimed invention is not considered routine in the art and without sufficient guidance to a specific combination; the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731 , 8 USPA2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

The specification fails to define what constitutes operable embodiment. It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

Given the above analysis of the factors, which the courts have determine are critical in determining whether a claimed invention is enabled, it would have taken one skilled in the art an undue and excessive experimentation in order to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 60-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "combination thereof" in claims 60-62 is a relative term, which renders the claim indefinite. The term "combination thereof" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of the term are not defined because the claims do not define what combination is being claimed. For example, in claims 60 and 62, the claims do not define whether the combination is a combination of therapeutic agents, cell cycle inhibitors, and/or vectors.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, SPE - Art Unit 1635, can be reached at (571) 272-0760.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER